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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,780	07/21/2006	Yong-Chul Kim	1942/65	1589

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KENYON & KENYON LLP
1500 K STREET N.W.
SUITE 700
WASHINGTON, DC 20005

EXAMINER	
YOUNG, SHAWQUIA	
ART UNIT	PAPER NUMBER
1626	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/586,780	KIM ET AL.	
	Examiner	Art Unit	
	Shawquia Young	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-3 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-3 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 21 July 2006 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-3 are currently pending in the instant application.

I. *Priority*

The instant application is a 371 of PCT/KR05/00209, filed on January 26, 2005 and claims benefit of Foreign Application REPUBLIC OF KOREA 10-2004-0005114, filed on January 26, 2004.

II. *Information Disclosure Statement*

Applicants' have not filed an Information Disclosure Statement.

III. Rejections

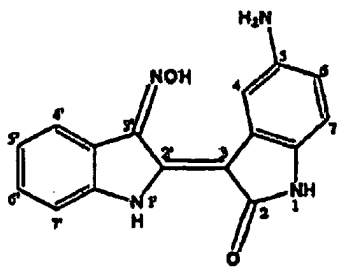
Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

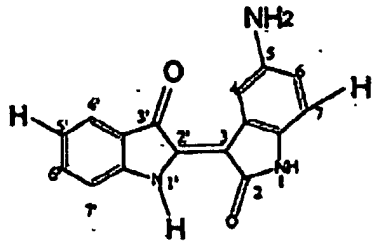
A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by *Eisenbrand* (WO 2000061555). The instant invention is drawn to an indirubin compound



representing various formulas such as and



The *Eisenbrand* reference teaches indirubin derivatives such as 5-amino-3-[1,3-dihyro-3-(hydroxyimino)-2H-indol-2-ylidene]-1,3-dihydro-2H-indol-2-one (See RN 301323-91-1, CAPLUS) and 5-amino-3-(1,3-dihyro-3-oxo-2H-indol-2-ylidene)-1,3-dihydro-2H-indol-2-one (See RN 301323-78-4, CAPLUS) and for pharmaceutical use in the treatment of solid cancers. This both of these compounds anticipate the genus compound of the instant invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, while the specification is enabling for the following human cancer cell lines: human lung cancer cell line, human stomach cancer cell line, human colon cancer cell line, human abdominal cavity cancer cell line and human leukemia cell line, it does not provide enablement for other human cancer cell lines. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in

the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01 (a), "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue".

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have need described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case,

The nature of the invention

The nature of the invention is an indirubin compound having anti-cancer property to human cancer cell line and property for inducing apoptosis to leukemia cell line by inducing differentation as CDK inhibitor representing the following formulas (I)-(VII).

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific disease by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic effects of all the encompassed cancers by inhibiting CDK would make a difference.

Applicants are claiming an indirubin compound having anti-cancer property to human cancer line.

Applicants' claims embrace all types on human cancer line but does not provide enablement for any human cancer line.

The state of the prior art is that cancer therapy remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular

mechanisms, and consequently, differ in treatment protocol. Cancer is a disease characterized by a population of cells that grow and divide without respect to normal limits, invade and destroy adjacent tissues, and may spread to distant anatomic sites through a process called metastasis (URL:http://en.wikipedia.org/wiki/ Cancer>). Most cancers are named for where they start. For example, lung cancer starts in the lung, and breast cancer starts in the breast. Symptoms and treatment depend on the cancer type and how advanced it is ((<URL:http://www.nlm.nig.gov/medlineplus/print/> cancer.html>). It is known that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, that cancer classification has been based primarily on morphological appearance of the tumor and that tumors with similar histopathological appearance can follow significantly different clinical courses and show different responses to therapy (Golub et al. page 531). Treatment may include surgery, radiation, chemotherapy, immunotherapy, monoclonal antibody therapy, etc. Furthermore, it is known that chemotherapy is most effective against tumors with rapidly dividing cells and that cells of solid tumors divide relatively slowly and chemotherapy is often less effective against them. It is also known in the prior art (Lala et al. page 91) that the role of NO in tumor biology remains incompletely understood with both the promotion and inhibition of NO mentioned for the treatment of tumor progression and only certain human cancers may be treated by selected NO-blocking drugs. These example shows that there are different cellular mechanisms, the unpredictability in the art and the different treatment protocols. Because "cancer" refers to a class of diseases, it is unlikely that there will ever be a single "cure or treatment for

cancer".

There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The amount of direction present and the presence or absence of working examples

Applicants have listed what human cancer lines have been used in the assay for analysis of inhibition effect to cancer cell line proliferation by indirubin derivative. Applicants specifically tested the following human cell cancer lines: human lung cancer cell line, human stomach cancer cell line, human colon cancer cell line, human abdominal cavity cancer cell line and human leukemia cell line.

Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved." See In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The breadth of the claims

The breadth of the claims is drawn to an indirubin compound having anti-cancer property to human cancer cell line and property for inducing apoptosis to leukemia cell line by inducing differentation as CDK inhibitor representing the following formulas (I)-(VII).

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what human cancer cell line out of all the numerous types of cancer would be benefited by the inhibition of CDK would furthermore then have to determine which of the claimed compounds in the instant invention would have what type of anti-cancer property.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* or *in vivo* screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and In re Fisher (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which type of cancers can be treated by the compound encompassed in the instant claims, with no assurance of success.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 and 3 recites the limitation "at least one compound represented by above formulas (I)-(VII)" but does not depend on claim 1 which contains the structure of the formulas. There is insufficient antecedent basis for this limitation in the claim.

IV. *Objections*

Claim Objections

Claims 1 and 2 are objected to because of the following informalities: there should be the term "or" between formulas VI and VIII in claims 1 and 2. Claim 1 is missing a period at the end of the claim. The period should be at the end of the structures. Each claim begins with a capital letter and ends with a period (MPEP 608.01 (m)). Appropriate correction is required.

V. *Conclusion*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shawquia Young whose telephone number is 571-272-9043. The examiner can normally be reached on 6:30 AM-3:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's

supervisor, Joseph McKane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

KAMAL A. SAEED, PH.D.
PRIMARY EXAMINER

Shawquia Young
Patent Examiner
Art Unit 1626, Group 1620
Technology Center 1600

Kamal Saeed
Primary Patent Examiner
Art Unit 1626, Group 1620
Technology Center 1600